

## LETTER TO THE EDITOR

## Recurrent injection-site reactions after incorrect subcutaneous administration of a COVID-19 vaccine

To the Editor,

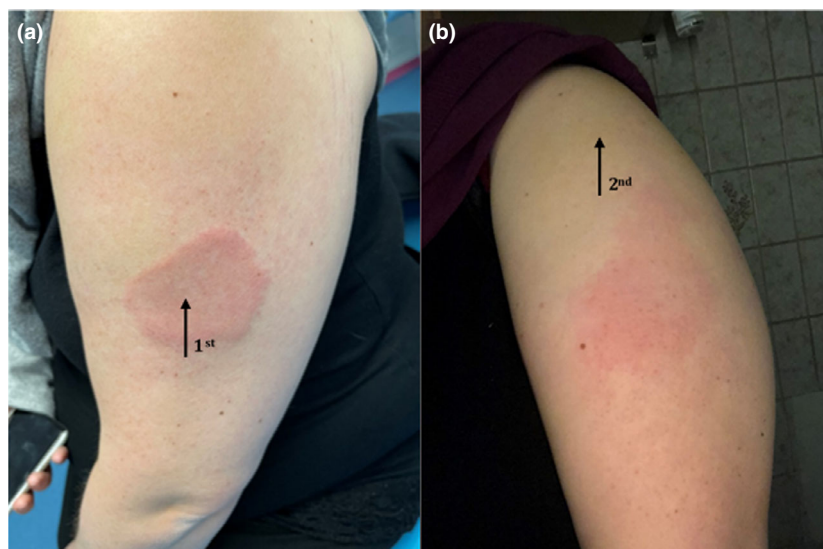
Local reactions to SARS-CoV-2 vaccination are common and mainly occur within the first week, albeit also seen later.<sup>1</sup> Here, we address another aspect of cutaneous side effects to SARS-CoV-2 vaccination and draw attention to implications in clinical practice.

A 33-year-old woman with type-2 diabetes and obesity (BMI 43 kg/m<sup>2</sup>) was incorrectly given the first SARS-CoV-2 vaccination dose (BNT162b2, Pfizer-BioNTech) in the middle of her left upper arm. There were no complications to the procedure. One week later, she developed fever, myalgia, arthralgia and malaise and tested PCR-positive for SARS-CoV-2. Five days after symptom onset, she noticed an asymptomatic rash at the injection site (Fig. 1a). A lesional 3 mm skin punch biopsy showed perivascular lymphocyte infiltration in the dermis. Using ELISA,<sup>2</sup> serology testing performed on postvaccination day 13 and 35 initially demonstrated an IgG response towards the receptor-binding domain (RBD) of the spike protein but was negative for response against

viral N-protein. At follow-up, antibodies against both RBD and viral N-protein were detected. The rash disappeared without treatment. Following correct re-vaccination in the left deltoid, the patient, within hours, developed skin erythema, intense soreness and warmth at the first injection site (Fig. 1b). The exanthema cleared spontaneously within a few days.

In this case, the first SARS-CoV-2 vaccine dose was accidentally injected subcutaneously due to incorrect anatomical location and high patient BMI. The significant skin reactions at the original injection site following SARS-CoV-2 infection and re-vaccination, respectively, are most likely caused by immunological reactivity towards vaccine antigens trapped in the subcutaneous tissue. As RBD is contained in the vaccine and N-protein is not, the patient's primary immune response was most likely raised against the vaccine, while both vaccine and virus antibodies were identified at follow-up.

Like most vaccines, SARS-CoV-2 vaccination should be administered intramuscularly to optimize immunogenicity and minimize local adverse reactions. Compared with muscle tissue, subcutaneous fat is less vascularized, which may harm the processing and presentation of antigens. In addition, superficial administration of vaccines more likely causes local side effects.<sup>3</sup> Obese individuals are at greater risk for severe SARS-CoV-2 infection and seem to generate poorer humoral vaccination responses compared with normal-weight persons.<sup>4</sup> Therefore,



**Fig. 1** Local skin reactions, left upper arm (patient photographs). (a) Day 12 after first COVID-19 vaccination; day 5 after SARS-CoV-2 infection. (b) Day 48 after first BNT162b2 vaccination; few hours after COVID-19 re-vaccination; Arrows indicate the two injection sites.

correct administration of SARS-CoV-2 vaccines is essential in the obese population. Deltoid fat pad thickness varies greatly,<sup>5</sup> and vaccination needles should be chosen individually to ensure intramuscular bioavailability.

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### Conflict of interest

None.

M. Gyldenløve,<sup>1,\*</sup>  L. Skov,<sup>1</sup>  C.B. Hansen,<sup>2</sup> P. Garred<sup>2</sup>

<sup>1</sup>Department of Dermatology and Allergy, Herlev and Gentofte Hospital, University of Copenhagen, Hellerup, Denmark, <sup>2</sup>Laboratory of Molecular

Medicine, Department of Clinical Immunology, Section 7631, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

\*Correspondence: M. Gyldenløve. E-mail: mette.gyldenloeve@regionh.dk

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